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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,836	05/10/2006	Junho Chung	Q94845	2218

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EXAMINER	
WEN, SHARON X	
ART UNIT	PAPER NUMBER
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,836	CHUNG ET AL.	
	Examiner	Art Unit	
	Sharon Wen	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *1-4,9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/10/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III in the reply filed on 03/28/2007 is acknowledged. The traversal is on the ground(s) that Groups I to IV form a single general inventive concept and should be examined altogether. This is not found persuasive for reasons stated in the Restriction Requirement. Applicant disagrees with the examiner's identification of the feature uniting the inventions as drawn to a neutralizing antibody which binds to a neaturalizable epitope of HGF. Applicant asserts that the uniting technical feature of the subject application is a neutralizing antibody which can neutralize HGF as a single agent and inhibit cell scattering activity by binding to the unique neutralizable epitope of claim 1. However such features are not recited in the claims.

The requirement is still deemed proper and is therefore made FINAL.

Upon further consideration, species election is extended to include antibody with V_H and V_L regions of amino acid sequence of SEQ ID NO: 27 and 28, respectively, in the interest of compact prosecution.

2. Claims 1-10 are pending.

Claims 5-8 are currently under examination as they read on a neutralizing antibody.

Claims 1-4 and 9-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 03/28/2007.

Priority

3. The effective priority date for claims 5-8 is deemed the filing of PCT/KR04/02888, i.e. 11/09/2004.

Applicant is invited to amendment the first line of the specification to recite Applicant's claim for benefit of PCT/KR04/02888.

Information Disclosure Statement

4. The information disclosure statement filed 05/10/2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Specification

5. The use of the trademark has been noted in this application (e.g. see page 16 lines 17, "NuPAGE"). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

6. Claims 5-8 are objected to because of the following informalities: claims 5-8 depend from a non-elected claim, claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 5-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 5-8, as written, do not sufficiently distinguish over nucleic acids, proteins, cells and antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as disclosed in the specification. See MPEP 2105.

The claims recite a neutralizing antibody which binds to a neutralizable epitope of HFG. The antibody is not recited as isolated or purified and hence reads on a naturally occurring autoantibody that binds to HGF.

Applicant is invited to amend the claims to recite "isolated" before neutralizing antibody to obviate this rejection given there is sufficient written support in the specification.

Claim Rejections - 35 USC § 112 second paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 5-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5-8 are indefinite in the recitation "neutralizable epitope" because the metes and bounds of the "neutralizable" characteristic of said epitope is unclear and ambiguous.

It is suggested to amend the claim to recite the particular characteristics intended, provided there is written description in the specification as filed.

Claim Rejections - 35 USC § 112 first paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant discloses in the specification that the neutralizing antibodies of the present invention is capable of neutralizing HGF as a single agent by binding to a neutralizable epitope on HGF (page 3 lines 3-4 of the instant specification). However the disclosure in the specification does **not** support the claims put forth by the Applicant to show that the Applicant is in possession of an antibody that binds to a neutralizable epitope of HGF **having** the amino acid sequence of SEQ ID NO:32 or 33 as recited in claim 1 for the following reason:

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C § 112, paragraph 1 "Written Description" requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January, 2001, See especially page 1106 3rd column).

The present claims recites a neutralizable epitope of HGF **having** the amino acid sequence set forth in the claim. The term "**having**" in the instant claims is open-ended and extends the epitope to include additional non-disclosed sequences on either or both sides of the disclosed region. As the term "having" is applied to sequences other than full length HGF, there does not appear to be sufficient written description in the specification as filed to convey to the

skilled artisan that the inventors, at the time the application was filed, had possession of the claimed genus of neutralizing epitopes.

Similarly Applicant has not provided a sufficient written description of an antibody that selectively binds to the genus of epitopes, because such antibody would not reasonably be expected to be reactive with the variants of epitopes. For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991; see entire document) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody. Further, Li et al. (PNAS 77: 3211-3214, 1980; see entire document) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document). Therefore, the specification does not provide for sufficient written description to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of antibodies to any epitope **having** the amino acid sequence of SEQ ID NO:32 or 33, other than the antibodies that binds to the epitope of SEQ ID NO:32 or 33.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

13. Claims **5-8** are rejected **under 35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated above, the claims of the present application are directed to a neutralizing antibody that binds a neutralizable epitope of HGF. However, the specification does not provide a suffienct enabling description of a neutralizing antibody that binds of a genus of neutralizable epitope of HGF **having** the amino acid sequences of SEQ ID NO:32 or 33 for the following reason:

The term "**having**" in the instant claims is open-ended and extends the epitope to include additional non-disclosed sequences on either or both sides of the disclosed region. As the term "**having**" is applied to sequences other than full length HGF, there does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various fragments encompassed by the instant claims. A person of skill in the art would not know which sequences are neutralizing, which sequences are non-neutralizing, and what particular sequence lengths identify neutralizing sequences. Without detailed direction as to which amino acid sequences are essential for neutralization, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of polypeptide sequences encompassed by the instant claims would share the neutralizing function of SEQ ID NO:32 or 33.

Because the neutralizable epitopes are the targets of the claimed antibodies, thus the antibody is not enabled as well. Applicant has not provided a sufficient enabling description of an antibody that selectively binds to such variant neutralizable epitopes, because such antibody would not reasonably be expected to be reactive with the epitope of SEQ ID NO:32 or 33. For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991; see entire document) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody. Further, Li et al. (PNAS 77: 3211-3214, 1980; see entire document) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document). Therefore, the specification does not provide for sufficient enablement for antibodies reactive with genus of epitopes **having** the amino acid sequence of SEQ ID NO:32 or 33 other than those reactive with the epitope of SEQ ID NO:32 or 33.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working

examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Cao et al. (*PNAS*, 2001, 98:7443-7448, cited in the Requirement for Restriction mailed 01/29/2007, see entire document).

The present claims are directed to a neutralizing antibody binding to a neutralizable epitope of HGF having the amino acid sequence of SEQ ID NO:32 or 33. Because of the open-ended term "having" recited in the present claims, under the broadest reasonable interpretation, the present claims read on a neutralizing antibody that binds to HGF. Cao et al. teaches a neutralizing antibody binding to HGF containing the neutralizable epitope of SEQ ID NO:32 or 33, wherein the antibody is a monoclonal antibody (e.g. see Introduction and Materials and Methods, page 7443, column 2, paragraphs 3 and 5).

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Wen whose telephone number is (571) 270-3064. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on (571) 272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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May 21, 2007

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